What is the relationship between the intake of animal protein products and breast cancer?

Conclusion

Limited evidence from cohort studies shows there is no association between the intake of animal protein products and overall breast cancer risk. However in sub-groups of breast cancer patients, limited evidence suggested a relationship between the intake of animal protein products and risk of developing breast cancer.

Grade: Limited

Overall strength of the available supporting evidence: Strong; Moderate; Limited; Expert Opinion Only; Grade not assignable For additional information regarding how to interpret grades, click here.

Evidence Summary Overview

This review included six studies published since 2000 (Cho, 2006; Ferrucci, 2009; Fung, 2005; Kabat, 2009; Linos, 2008; Taylor, 2007) representing prospective cohorts from the US and United Kingdom. Results were often reported based on menopausal status (pre-menopausal or post-menopausal) and estrogen receptor status (positive or negative). In the Nurses' Health Study (Cho, 2006), overall, there was no association between total meat intake and risk of breast cancer. However, there was a positive association for ER (estrogen receptor)+/PR (progesterone receptor)+ breast cancer and no association for ER-/PR-. Similarly, they reported positive associations between ER+/PR+ breast cancer and individual red and processed meats, but not for ER-/PR-. Ferrucii et al, 2009, found a stronger association between red meat intake and ER+/PR+ breast cancer compared to negative receptor status in the PLCO Screening Trial.

In additional analyses from the Nurses' Health Study, Linos et al, 2008, found a positive association between pre-menopausal breast cancer and red meat and this relationship was stronger among estrogen receptor positive participants. In the UK Women's Cohort Study (Taylor, 2007), positive associations between total meat and pre-menopausal and post-menopausal breast cancer were observed. Non-processed meat also was positively associated with pre-menopausal breast cancer. However, post-menopausal but not pre-menopausal breast cancer was associated with the intake of red meat and processed meat. Thus, results are conflicting and future research should further investigate the relationship between the intake of animal protein products and breast cancer specifically related to menopausal and receptor status.

Evidence Summary Paragraphs

Cho et al, 2006 (positive quality) evaluated the intake of red meat and breast cancer risk according to tumor hormone receptor status among 90,659 pre-menopausal women (aged 26 to 46 years) in the Nurses' Health Study II (US). Breast cancer was self-reported by biennial questionnaires mailed between 1993 and 2003 and confirmed by review of pathologic reports. A semi-quantitative food-frequency questionnaire (FFQ) with more than 130 food items was sent to women in 1991, 1995 and 1999 to assess usual dietary intake during the past year. Total red meat and individual red meat items were included in analyses. During 12 years of follow-up, 1,021 cases of invasive breast carcinoma were identified. The highest intake of red meat was weakly and non-significantly (NS) associated with elevated risk of overall breast cancer. Greater red meat intake was strongly related to elevated risk of breast cancers that were estrogen and progesterone receptor positive (ER+/PR+; N=512), but not to those that were estrogen and progesterone receptor negative (ER-/PR-; N=167). Compared with those eating three or fewer servings per week of red meat, the multi-variate relative risks for ER+/PR+ breast cancer with increasing servings of red meat intake were 1.14 (95% CI: 0.90, 1.45) for more than three to five or fewer servings per week, 1.42 (95% CI: 1.06, 1.90) for more than five per week to one or fewer servings per day, 1.20 (95% CI: 0.89, 1.63) for more than 1 to 1.5 or

fewer servings per day and 1.97 (95% CI: 1.35, 2.88) for more than 1.5 servings per day (P=0.001). The corresponding relative risks (RR) for ER-/PR- breast cancer were 1.34 (95% CI: 0.89, 2.00), 1.21 (95% CI: 0.73, 2.00), 0.69 (95% CI: 0.39, 1.23) and 0.89 (95% CI: 0.43, 1.84) (P=0.28). No strong associations were found between individual red meat items and overall breast cancer risk; however, almost all of the individual red meat items had statistically significant positive trends of increasing ER+/PR+ breast cancer risk (beef or lamb as main dish, P=0.03; pork as main dish, P=0.005; hamburger, P=0.01; hot dogs, P=0.005; other processed meats, P<0.001). Individual red meat items were not positively related to ER-/PR- cancers. The authors concluded that higher red meat intake may be a risk factor for ER+/PR+ breast cancer among pre-menopausal women.

Ferrucci et al. 2009 (positive quality) used prospective cohort data from 52,158 women (55 to 74 years) participating in the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial (US) to investigate meat intake and potentially carcinogenic meat-related exposures in relation to post-menopausal invasive breast cancer. Incident cancer cases were identified through self-report from annual study update questionnaire, physician reports or through reports from the next of kin, and were histologically confirmed based on pathology reports and medical records. Meat intake was assessed at baseline using the Diet History Questionnaire, a self-administered, validated FFQ, which consisted of 124 items. Red meat, white meat and processed meat were included in analyses. During a mean follow-up of 5.5 years, 1,205 invasive breast cancer cases were identified. Comparing the fifth to the first quintile, red meat was positively associated with breast cancer (HR=1.23; 95% CI: 1.00, 1.51; P=0.22). Statistically significant or borderline-positive associations between red meat and breast cancer were observed starting in the second quintile, and there was no evidence for a dose-response effect (P=0.22), consistent with a potential threshold effect. When ER+ /PR+ tumors were compared to non-cases, the effect of red meat seemed to be stronger (O5 vs. O1 H = 1.59; 95% CI: 1.03, 2.48; P=0.09). There were NS associations with processed meat, white meat or individual meat items. Pan-fried meat, grilled meat and well/very well done meat were not associated with breast cancer risk. The authors concluded that their results support an association between red meat and post-menopausal breast cancer.

Fung et al, 2005 (positive quality) examined the relationship between dietary patterns and breast cancer in 71,058 post-menopausal women from the Nurses' Health Study (US). Post-menopausal breast cancer was determined by self-report in biennial questionnaire. A total of 99% of cases were confirmed by reviewing medical records. Dietary intake was assessed using the 1984 FFQ that consisted of 116 items. Two major dietary patterns were identified (prudent and Western). The prudent pattern was characterized by higher intake of fruits, vegetables, whole grains, low-fat dairy products, fish and poultry, while the Western pattern was characterized by higher intake of red and processed meats, refined grains, sweets and desserts and high-fat dairy products. Separate analyses considered the relationship between individual food items (including processed meats, red meats and poultry) and estrogen receptor-negative (ER-) breast cancer. Between 1984 and 2000, 3,026 incident cases of post-menopausal breast cancer were ascertained. Neither of the dietary patterns was associated with overall risk of post-menopausal breast cancer. However, a positive association between the Western pattern score was observed among smokers at baseline [RR = 1.44, comparing top to bottom quintiles; 95% CI: 1.02, 2.03; P=0.03). An inverse association was observed between the prudent pattern and ER- cancer (RR=0.62; 95% CI: 0.45, 0.88; P=0.006). No significant relationships between processed meats, red meats or poultry and ER- breast cancer were observed. (Relationships between processed meats, red meats or poultry and ER+ or overall breast cancer risk were not reported.) The authors concluded that they did not observe an overall association between the prudent or Western pattern and overall breast cancer risk.

Kabat et al, 2009 (positive quality) examined the association between meat, meat-cooking methods, and meat-mutagen intake and post-menopausal breast cancer in the National Institutes of Health-American Association for Retired Persons (NIH-AARP) Diet and Health Study cohort (N=120,755). Breast cancer cases were identified by linking cohort members to state cancer registries and to the US National Death Index between 1995 and 2005. Dietary intake was assessed at baseline using a self-administered FFQ with 124 items. Within six months following the initial questionnaire, participants were sent a second FFQ that included a meat-cooking module. The meat-cooking module queried consumption of hamburgers, steak,

bacon and chicken, usual cooking method and level of doneness on the outside and inside. During eight years of follow-up, 3,818 cases of invasive breast cancer were identified. Intake of total meat, red meat, meat cooked at high temperatures and meat mutagens showed no association with breast cancer risk. No significant associations were seen by hormone receptor status (ER+, ER-, PR+, PR-) for intake of total meat, red meat, meat cooked at high temperatures or five indicators of mutagenic activity. Breast cancer risk was not associated with high-temperature cooking methods or level of doneness. The authors concluded that the results of this prospective study do not support the hypothesis that a high intake of meat, red meat, processed meat, meat cooked at high temperatures or meat mutagens is associated with increased risk of post-menopausal breast cancer.

Linos et al. 2008 (positive quality) assessed the relationship between red meat intake during adolescence and pre-menopausal breast cancer risk among 39,268 participants from the Nurses' Health Study II (US). Breast cancer incidence was ascertained on biennial follow-up questionnaires and confirmed by medical records and pathology reports. In 1991 and 1995, participants completed a semi-quantitative FFQ of usual dietary intake during the past year. The mean of the 1991 and 1995 FFQ was used to estimate current adult red meat intake. Individual red meat items included beef or lamb as a main dish; pork as a main dish; beef, pork, or lamb as a sandwich or mixed dish; hamburger; bacon; hot dogs; and other processed meats. Adolescent diet was assessed retrospectively with a 124-item FFQ on diet during high school. This questionnaire was specifically designed to include foods that were commonly consumed from 1960 to 1980. The adult and high school FFQs included the same red meat items. From 1998 to 2005, 455 cases of invasive pre-menopausal breast cancer were diagnosed. Compared with women in the lowest quintile of red meat intake during high school, the multi-variate-adjusted RR for the highest quintile of intake was 1.34 (95% CI: 0.94, 1.89; P=0.05). When individual red meats were considered, there was a significant association for frequent hot dog consumption in high school and breast cancer risk (RR=1.36; 95% CI: 0.95, 1.95; P=0.03). No significant associations were observed for bacon; beef, pork or lamb sandwich or stew; meatloaf; beef or lamb as main dish; hamburger; or pork as a main dish. A borderline significant association was observed for processed meat (P=0.07). A significant linear association was observed with every additional 100 g of red meat consumed per day (RR=1.20; 95% CI: 1.00, 1.43; P=0.05). This association was more pronounced in ERand PR-positive cancer (RR=1.36; 95% CI: 1.08, 1.70; P=0.008) and was not significant in ER- and PR-negative tumors (RR=0.99; 95% CI: 0.61, 1.61; P=0.97). The authors concluded that higher red meat intake in adolescence may increase the risk of pre-menopausal breast cancer.

Taylor et al, 2007 (positive quality) assessed the effect of meat consumption and meat type on the risk of pre- and post-menopausal breast cancer in the UK Women's Cohort Study (N=33,725). To determine cancer status, details of women fulfilling the eligibility criteria were submitted to the UK Office of National Statistics and subsequently flagged on the NHS central register. Dietary intake was assessed with a 217-item FFQ. Meats considered included red meat, poultry, offal and processed meat. During a median follow-up of eight years, a total of 1,750 incident malignant cancer cases were recorded, including 283 pre-menopausal and 395 post-menopausal breast cancers. High consumption of total meat compared with none was associated with pre-menopausal breast cancer (HR=1.20; 95% CI: 0.86, 1.68) and high non-processed meat intake compared with none (HR=1.20; 95% CI: 0.86, 1.68). The estimated RR of pre-menopausal breast cancer for an increase in total meat consumption of 50g per day was 1.12 (95% CI: 1.02, 1.23; P=0.02). RR of non-processed meat per 50g per day was 1.13 (95% CI: 1.01, 1.26; P=0.03). The association of pre-menopausal breast cancer with processed meat and red meat was not statistically significant. Total meat intake was positively associated with post-menopausal breast cancer, HR=1.63 (95% CI: 1.10, 2.30) for high consumption vs. the reference category, and when treated as a continuous variable, resulted in a significant linear trend and relative risk per 50g per day of 1.10 (95% CI: 1.01, 1.20; P=0.02). Relationships between both processed meat and red meat and post-menopausal breast cancer were also significant. Risks for the three meat types were similar when considering HRs of the categorical analysis; however, fitting meat in the model as a continuous predictor resulted in a much stronger relationship with processed meat, giving an RR per 50g per day of 1.64 (95% CI: 1.09 to 2.27, P=0.003). The authors concluded that women, both pre- and post-menopausal, who consumed the most meat had the highest risk of breast cancer.

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Author, Year, Study Design, Class, Rating	Study Name/Location	Total Meat Association (Pos, Neg, None)	Red Meat (Pos, Neg, None)	Processed Meat (Pos, Neg, None)	Poultry (Pos, Neg, None)
Cho et al 2006 Study Design: Prospective cohort study Class: B Rating:	Nurses' Health Study. Location: US.	Ø Overall. (+) ER+/PR+. Ø ER-/PR	Beef or lamb as main dish; pork as main dish; hamburger: (+) ER+/PR+ only.	Hot dogs: (+) ER+/PR+ only. Other processed meats: (+) ER+/PR+ only.	Not examined.
Ferrucci LM, Cross AJ et al, 2009 Study Design: Prospective Cohort Study Class: B	Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial. Location: US.	Doneness: Ø.	(+) with stronger association for ER+/PR+.	Ø.	White meat: Ø.
Rating: Fung et al 2005 Study Design: Prospective Cohort Study Class: B Rating: Fung et al 2005	Nurses' Health Study. Location: US (results presented here only represent ER- cancer).	Not examined.	Ø ER	Ø ER	Ø ER
Kabat et al 2009 Study Design: prospective cohort study Class: B	NIH-AARP Diet and Health Study. Location: US (study only included post-menopausal women).	Ø Post-menopausal BC (including analyses with ER/PR status). Doneness: Ø Post-menopausal BC.	Ø Post-menopausal BC (including analyses with ER/PR status).	Not examined.	Not examined.

Rating:					
Linos et al 2008 Study Design: prospective cohort study Class: B Rating:	Nurses' Health Study II. Location: US (study only included pre-menopausal women).	Not examined.	(+) Pre-menopausal BC with stronger association for ER+/PR+ (Ø for ER-/PR-) (Ø for individual food items).	Hot dogs: (+) Pre-menopausal BC. (Ø for other individual food items).	Not examined.
Taylor et al 2007 Study Design: Prospective Cohort Study Class: B Rating:	UK Women's Cohort Study. Location: United Kingdom (study included pre- and post-menopausal women).	(+) Pre-menopausal and post-menopausal BC. Non-processed meat: (+) Pre-menopausal BC.	Ø Pre-menopausal BC. (+) Post-menopausal BC.	Ø Pre-menopausal BC. (+) Post-menopausal BC.	Not examined.

Research Design and Implementation Rating Summary

For a summary of the Research Design and Implementation Rating results, click here.

Worksheets

- Cho E, Chen WY, Hunter DJ, Stampfer MJ, Colditz GA, Hankinson SE, Willett WC. Red meat intake and risk of breast cancer among premenopausal women. Arch Intern Med. 2006 Nov 13;166(20):2253-9.
- Ferrucci LM, Cross AJ, Graubard BI, Brinton LA, McCarty CA, Ziegler RG, Ma X, Mayne ST, Sinha R. Intake of meat, meat mutagens, and iron and the risk of breast cancer in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial. *Br J Cancer*. 2009 Jul 7; 101(1): 178-184.
- Fung TT, Hu FB, Holmes MD, Rosner BA, Hunter DJ, Colditz GA, Willett WC. Dietary patterns and the risk of postmenopausal breast cancer. Int J Cancer. 2005;116:116-121.
- Kabat GC, Cross AJ, Park Y, Schatzkin A, Hollenbeck AR, Rohan TE, Sinha R. Meat intake and meat preparation in relation to risk of postmenopausal breast cancer in the NIH-AARP diet and health study.

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- Taylor EF, Burley VJ, Greenwood DC, Cade JE. Meat consumption and risk of breast cancer in the UK Women's Cohort Study. Br J Cancer. 2007 Apr 10;96(7):1139-46. Erratum in: Br J Cancer. 2007 Jun